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TITLE: Social Support and Endocrine Function: A Randomized Trial  
with Breast Cancer Patients

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<b>13. ABSTRACT (Maximum 200 Words)</b> <p>While there is clear evidence that psychological/behavioral interventions with cancer patients provide adjustment and coping benefits (Mark &amp; Meyer, 1995) as well as positive immune and survival benefits (Fawzy et al., 1993; Spiegel et al., 1989), the mechanisms for the benefits of such groups are not clearly understood. We propose that one of the mechanisms for the success of intervention groups may be through the provision of social support. Thus, by receiving needed support, patients may be "buffered" or protected from the more negative effects of the cancer stressor (e.g., depressive symptoms, Spiker, Trijsburg, &amp; Duivenvoorden, 1997; and immune down-regulation, Andersen et al., 1998). Therefore, we are studying the impact of a psychological/behavioral intervention with 231 breast cancer patients, using treatment (intervention) and control (no intervention) arms, on social support and endocrine responses.</p> <p>We found (1) The intervention participants do not have significantly higher levels of social support than the assessment only subjects. Although there are trends that suggest that the intervention participants maintain support levels while the assessment only subjects report lower support over time. (2) The intervention participants do have significantly lower levels of stress hormones than the assessment only subjects. Furthermore, psychological stress (ie., perceived stress and life events), across groups, is associated with depressive symptoms. (3) There is no support for the stress buffering hypothesis of social support in this sample. In fact, those women who belong to 1 or more groups show higher stress hormones in comparison to women who do not. However, women in the intervention, regardless of outside group participation, show stable or decreasing stress hormone levels over time. Intervention effects, however, over time (12-months), are not well-maintained and may well be related to transitioning from weekly meetings to monthly ones.</p>				
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## Introduction

While there is clear evidence that psychological/behavioral interventions with cancer patients provide adjustment and coping benefits (Mark & Meyer, 1995) as well as positive immune and survival benefits (Fawzy et al., 1993; Spiegel et al., 1989), the mechanisms for the benefits of such groups are not clearly understood. We proposed that one of the mechanisms for the success of intervention groups may be through the provision of social support. Thus, by receiving needed support, patients may be “buffered” or protected from the more negative effects of the cancer stressor (e.g., depressive symptoms, Spiker, Trijsburg, & Duivenvoorden, 1997; and immune down-regulation, Andersen et al., 1998). We proposed studying the impact of a psychological/behavioral intervention with breast cancer patients, using treatment (intervention) and control (no intervention) arms, on social support and endocrine responses. We also were interested in endocrine functioning as a biological marker of stress severity (Uchino, Cacioppo, & Kiecolt-Glaser, 1996) in breast cancer patients. Data from this study is being used to determine: (1) if an intervention is associated with significantly higher levels of social support among the intervention subjects, (2) if an intervention is associated with significantly lower endocrine stress responses among intervention subjects, and (3) test the stress buffering hypothesis of social support, that is test for an interaction between study arm (intervention vs. no intervention) and initial level of social support (high vs. low) across time (initial vs. post-treatment) on endocrine function (e.g., cortisol).

## Body

### A. Description of Training and Research Accomplishments to Date

The army funding, beginning in August 1997 (DAMD17-97-1-7062), has enabled the principal investigator to accomplish both research and professional goals, per the statement of work, as discussed below: Task 1 and Task 2 (Endocrine Panel Selection and Management), Task 3 (Management of Social Support Data), Task 4 (Professional Development), and Task 5 (Intervention Therapist).

**Task 1 and Task 2: Endocrine Panel Selection and Management.** I have meet regularly with Drs. Andersen and Malarkey over the past 3 years regarding endocrine data (collection, management, and analysis). These meetings have also included laboratory personnel as needed (e.g., proper collection of salivary cortisol). The final endocrine panel of the larger study included cortisol (CORT), prolactin (PRL), and growth hormone (GH) with results from frozen plasma, and epinephrine (EPI), norepinephrine (NEPI), and acetylcholine (ACTH) with results from fresh plasma. We also collected salivary cortisol (SCORT). Of course, the main endocrine stress marker, of interest to this study was plasma cortisol.

Table 1 provides the sample sizes of the various endocrine variables available for data analysis. Because EPI, NEPI, ACTH, and SCORT were not collected until later in the larger project, fewer data points are available for these variables. We have not experienced any

significant problems with “unusual” values within or across assays. All intra- and inter-assay coefficients of variation are 12% or lower. Because the endocrine data is run in batches to reduce inter-assay variation not all data points were available for analyses. Approximately another 40 data points will be added to the data set over the next year.

Table 1  
Endocrine Data Points Available for Statistical Analysis

	Initial	4-Month	8-Month	12-Month
CORT	166	140	146	143
GH	120	97	106	107
PRL	121	104	113	111
EPI	79	76	54	51
NEPI	80	71	52	49
ACTH	25	50	59	50
SCORT	46	55	65	65

**Task 3: Management of Social Support Data.** We have maintained checks on the collection, accuracy, and management of the social support data gathered through the larger study using regularly scheduled contacts (weekly staff meeting with research personnel). Note, eligible women are newly diagnosed and/or recently treated women with Stage II or III breast cancer. Following accrual, women are randomized between intervention and assessment only arms and followed every 4 months during the year, a total of 4 assessment time points. Again, we have not encountered any significant problems in data collection or management. For the present study, recruitment and accrual issues are not specific problems as the subjects are already participating in the larger study. In fact, the study dropout rate at 12 months of participation is extremely low at 6.5%. Thus, we have been very successful in keeping subjects in the study.

All total, in the larger study, we have collected data on 241 subjects (goal of 235) at the initial time point. Due to eligibility criteria, the final sample was reduced to 231 subjects at the initial assessment. Current numbers available for the 4-, 8-, and 12- month assessments are 181, 164, and 153, respectively. Data collection is only complete through the initial assessment and additional data points at the follow-up assessments will continue to be collected over the next 6 months.

Also, we have conducted analyses, as proposed, examining for potential bias between the intervention and assessment only arms at the initial assessment. We have found no significant differences between arms on sociodemographic (age, race, annual family income, years of education, marital/partner status) or randomization criteria (tumor size, number of positive lymph nodes, estrogen receptor status, menopausal status, and presence/absence of partner/spouse). Therefore, we have data to support that our results are not confounded by pre- intervention vs. assessment only group differences. The typical breast cancer patient in the study is a 50 year old (SD = 10.72) married Caucasian women with some college education and an annual family income of \$67,000 (SD = 70.84). As far as disease characteristics are concerned, the average patient was diagnosed with stage II breast cancer including a 3 centimeter tumor, 3 positive

lymph nodes (SD = 5.45), and positive estrogen receptor status. She is pre or peri menopausal as well. The typical treatment is a mastectomy, followed by chemotherapy and hormonal treatment.

**Task 4: Professional Development.** During the past 3 years, I received behavioral medicine training in the following areas:

(1) **Relevant Literature:** I have had extensive reading of and exposure to the PNI literature with additional focus on endocrine research (under the direction of Drs. Malarkey and Andersen). This reading has been important in the development of studies and preparation of presentations/manuscripts. In addition, Dr. Malarkey and myself are currently developing a study to examine prolactin values of breast cancer patients versus patients with non-cancerous conditions (e.g., prolactinomas, prolactinemia) and healthy controls. Also, I have had extensive reading of the cancer literature in general and the literature on stress and cancer more specifically. I have had additional reading of the PTSD literature/research in cancer populations.

(2) **Statistics:** Obtained training in CEFA, Comprehensive Exploratory Factor Analysis, a computer program for conducting factor analyses created by Dr. Michael Browne. This program was used to analyze stress measurement data from the larger project and we have an article under review for publication:

Golden-Kreutz, D., Frierson, G., Brown, M., & Andersen, B. (Under review). Measurement invariance in longitudinal clinical research: Perceived stress in women with breast cancer. *Psychological Assessment*.

(3) **Training Meetings:** Attended meetings of the Health Psychology Graduate Colloquium Series in the Department of Psychology. This Health Psychology Series emphasizes current research and professional issues in the field and is regularly attended by faculty, postdocs, and graduate students in psychology. Additionally, I presented a talk based on my clinical experience with medical patients.

Golden-Kreutz, D. (1997, November). *The role of health psychologists in the assessment and management of organ recipients: A case study of liver transplantation*. Paper presented at a meeting of the Health Psychology Graduate Colloquium Series, Department of Psychology, The Ohio State University, Columbus, Ohio.

I also, attended meetings of the PNI Journal Club for PNI faculty (e.g., Andersen, Malarkey, Kiecolt-Glaser, Glaser), graduate students, and medical residents across university departments (including medicine, immunology, endocrinology, psychology, oral biology). The goal of the journal club is to discuss/critique empirical work in the PNI field. I also presented to the Journal Club published data from the larger study, a publication (Andersen et al., 1998) in which I was involved.

Andersen, B.L., Farrar, W.B., Golden-Kreutz, D., Kutz, L.A., MacCallum, R., Courtney, M.E., & Glaser, R. (1998). Stress alters immune responses following surgical treatment for regional breast cancer. *Journal of National Cancer Institute*, 90, 30-36.

In addition, I attended a "Good Clinical Practice Course" for cancer researchers offered by the James Cancer Hospital and Solove Research Institute (July, 2000). This course emphasized the standards by which clinical trials should be designed, conducted, recorded, and reported. Specific topics included: obtaining informed consent, working with Institutional

Review Boards (IRBs) and sponsors, and investigator responsibilities (e.g., recording keeping).

(4) ***Graduate Student Training/Supervision:*** I have and continue to work with Dr. Andersen's clinical psychology graduate students in formulating research ideas, planning research projects, data analysis, and preparation of conference submissions and presentations. More specifically, I have been involved in several graduate research projects including: 1- PTSD symptomatology in women with breast cancer; and 2- the role of religion/spirituality in the well-being of breast cancer patients. Listed below are conference presentations given by graduate students I supervised:

Frierson, G., Golden-Kreutz, D., Browne, M., & Andersen, B. (2000, April). The construct independence of perceived stress and depressive symptoms. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.

Pingel, K., Golden-Kreutz, D., Petri, M., & Andersen, B. (2000, April). Anxiety sensitivity: Its relationship to mood, social support, and somatic symptomatology in women post-adjuvant treatment for breast cancer. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.

(5) ***Editorial Experiences:*** Over the past 3 years I have had the opportunity to be an ADHOC Reviewer for the following Peer-reviewed Journals: "Health Psychology", "Journal of Consultation and Clinical Psychology," "Annals of Behavioral Medicine," and "Psychological Assessment" as well as a reviewer of abstracts submitted for the following conferences: Annual Meeting of the Society of Behavioral Medicine (1998) and the APA sponsored conference "Enhancing Outcomes in Women's Health: Translating Psychosocial and Behavioral Research into Primary Care, Community Interventions, and Health Policy" (2001). These review experiences have not only provided me with opportunities to read other researchers work but to also be more thorough and critical in my own thinking about research design, methods, analysis, and interpretation.

(6) ***Professional Identity:***

***Conferences:*** For further behavior medicine training I also attended the following conferences/invited presentations: Barbara Rimer, DR.P.H, invited address ("Cancer Risk and the Impact of Genetic Testing") at the James Cancer Hospital and Solove Research Institute, Columbus, Ohio (February, 1998), and Psychosocial Interventions and Cancer Conference at the University of Pittsburgh Cancer Institute, Pittsburgh, PA (October, 1998). I was also active in additional professional development activities (e.g., expanding collegial contacts, and presenting research findings at national/international meetings). References of presentations, chapters, and papers I was involved in writing or am currently in the process of writing not otherwise listed in Section 5: Body are listed below and all work is summarized in Section 7: Reportable Outcomes.

Golden-Kreutz, D., Frierson, G., Brown, M., & Andersen, B. (Under review). Measurement invariance in longitudinal clinical research: Perceived stress in women with breast cancer. Psychological Assessment.

Golden-Kreutz, D., & Andersen, B. (Invited to submit as Brief Report). Correlates of depressive symptoms in women with regional breast cancer: Examining objective versus subjective stress after surgery. Health Psychology.

*Golden-Kreutz, D., DeLamatre, M., Malarkey, W., & Andersen, B. (2000, June). The impact of a psychological/behavioral intervention on social support and endocrine function in women with breast cancer. Invited Platform Presentation and Poster presented at the Era of Hope Meeting sponsored by the Department of Defense Breast Cancer Research Program, Atlanta, Georgia.*

*Golden-Kreutz, D., Courtney, M., DiLillo, V., & Andersen, B. (2000, April). Objective stressors vs. subjective stress and their relationship to depressive symptoms: Examining the psychological responses to breast cancer diagnosis and treatment. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.*

*Golden-Kreutz, D., Farrar, W., & Andersen, B. (1999, March). Conducting clinical research with breast cancer patients: Issues of recruitment and retention. Poster presented at the 2nd Annual meeting of □Women succeeding in Science in 1999: A Multidisciplinary Poster Session□ sponsored by the Association for Women in Science of Central Ohio, The Ohio State University Office of Research, College of Biological Sciences and the Battelle Endowment for Technology and Human Affairs, Columbus, Ohio.*

*Golden-Kreutz, D., DiLillo, V., Farrar, W., & Andersen, B. (1998, July). The benefits of cognitive/behavioral interventions for women with breast cancer. World Congress of Behavioral and Cognitive Therapies, Acapulco, Mexico.*

*Andersen, B., & Golden-Kreutz, D. (2000). Sexual-self concept for the woman with cancer: An Update. In L. Baider, C. Cooper, & A. Kaplan De-Nour (Eds.) Cancer and the Family (2nd ed), England: Wiley & Sons.*

*Andersen, B.L., Golden-Kreutz, D., & DiLillo, V. (2000). Cancer, In A. E. Kazdin (Ed.), Encyclopedia of Psychology. Washington, DC: American Psychological Association Press.*

*Andersen, B.L., & Golden-Kreutz, D. & DiLillo, V. (1999). Cancer, In A. Baum, T. Revenson, & J. Singer (Eds.), Handbook of Health Psychology, NY: Erlbaum.*

*Andersen, B.L., & Golden-Kreutz, D. (1998). Cancer, In A.S. Bellack & M. Hersen (Eds.), Comprehensive Clinical Psychology: Health Psychology (Vol.7), NY: Elsevier Science.*

*Golden-Kreutz, D., Malarkey, W., & Andersen, B. (prepare for publication). Social support and endocrine functioning in women with breast cancer.*

*Golden-Kreutz, D., Thornton, L., Frierson, G., Lawrence, H., Wells, S., & Andersen, B. (prepare for publication). Negative changes in quality of life with the stress of cancer diagnosis and treatment.*

***Community Involvement:*** I have also discussed/presented research findings as well as the role of psychologists to the public including cancer patients and their families, other health professionals (e.g., nurses, mammographers), and undergraduate college students. This has provided me with an opportunity to present to groups of people outside my own discipline and learn about their interests and concerns related to cancer research. These talks are listed below:

*Golden-Kreutz, D. (2000, March). Use of psychological/behavioral interventions to reduce stress and enhance coping during breast cancer. Paper presented for the Student Nurses Association of Mt. Carmel Hospital and Mt Carmel Alumni Association Continuing Education Program (Nurses receive CEU credits for attending). Mount Carmel College of Nursing Lodge, Columbus, Ohio.*

*Golden-Kreutz, D. (1999, November). Member of professional panel speaking to undergraduate Psi Chi members regarding graduate training and occupational opportunities in the field of Psychology. Meeting at The Ohio State University, Columbus, Ohio.*

*Golden-Kreutz, D. (1999, October). Circle of supports. Workshop presented to cancer patients, family members, and staff at The Wellness Community, Columbus, Ohio. Workshop focused on ways of improving social support.*

*Golden-Kreutz, D. (1999, October). The Stress and Immunity Breast Cancer Project: Intervention effectiveness. Paper presented at a Mammography Seminar sponsored by the Central Ohio Society of Mammographers (Certified Mammographers receive CEU credits for attending), The James Cancer Hospital and Solove Research Institute, Columbus, Ohio.*

*Golden-Kreutz, D. (1998, November). The Stress and Immunity Breast Cancer Project: A research update. Paper presented at a meeting of the Spirit of Women Brown Bag Luncheon Series sponsored by the The National Center of Excellence in Women's Health, The Ohio State University Medical Center, Columbus, Ohio.*



**Task 5: Intervention Therapist.** I continue to be the lead co-therapist for the larger project. To date, I have lead all 12 intervention groups (11 through the entire one year intervention). The larger project will have 12 groups total. As a licensed psychologist I operate independently in leading the group and collecting process data. As necessary I confer with Dr. Andersen regarding group processes and/or data issues. I have also spent the last 3 years training advanced level clinical psychology graduate students in conducting the group intervention. In the training of students, we have weekly supervision meetings regarding group process, therapeutic techniques, and teaching cognitive/behavioral stress management skills to women with breast cancer. As the group therapist, I have gained skills as a psychotherapist, group therapist, and supervisor/teacher.

### **B. Analysis of Hypotheses to Date**

We have run analyses on all three of our hypotheses proposed for study using the initial, 4- and 12-month data. We will continue to run analyses using all the data points as more data become available and are added to the data set. Thus, continuing to add additional numbers will increase the reliability of our results. Below, for each hypothesis we ran two sets of analyses, one set included the initial and 4-month data and the second set included the initial and 12-month data. We did this to assess potential differences between groups at the end of the intensive phase of the intervention (4 months) and then again at the end of complete intervention (12 months).

**Hypothesis 1:** Do the intervention participants report significantly higher levels of social support than the assessment only subjects over time?

The following social support measures were used:

The Social Network Index (SNI; Cohen, 1991) assesses social integration and is potentially less subject to mood-related biases than perceptions of support. This measure assesses the number of people with whom the patient had contact on a regular basis and the number of important roles patients fulfill (e.g. spouse, parent, child, employee, friend, neighbor). The number of roles and the number of relationships across roles are predictors of mortality in epidemiologic studies (e.g. Berkman & Syme, 1979; House et al., 1982). The internal consistency of the SNI is .65.

The Perceived Social Support From Friends (PSS-Fr) & Family (PSS-Fa) are two 20-item instruments designed to measure the degree to which subjects' needs for support are fulfilled by their network of friends and family (Procidano & Heller, 1983). Sample items include, "My friends give me the moral support I need," and "I have a deep, sharing relationship with a number of members of my family." Total scores range from 0 to 20 for both scales, with higher scores reflecting more perceived social support. Internal consistency for the PSS-Fa and PSS-Fr ranges from .88 to .91 and .84 to .90, respectively. Test-retest reliability over a one-month period is .83 and factor analysis suggests the instruments each measure a single domain (Procidano & Heller, 1983). The specific variables studied are list below in Table 2:

Table 2

Social Support Variables Studied

SO (Presence/absence of significant other)

SNI (Social Network Index-total score) and the following subscales:

NFAM-Number of family members available

NFR-Number of friends available

GRPS-Number of groups (e.g., PTA, social, organizational) belong to

SOC-Sociability (combination score of the number of relatives and close friends and monthly contact with these people)

GRPATT- How often you attend group meetings (0 = almost never, 2 = about once a month, 4 = more than once a week)

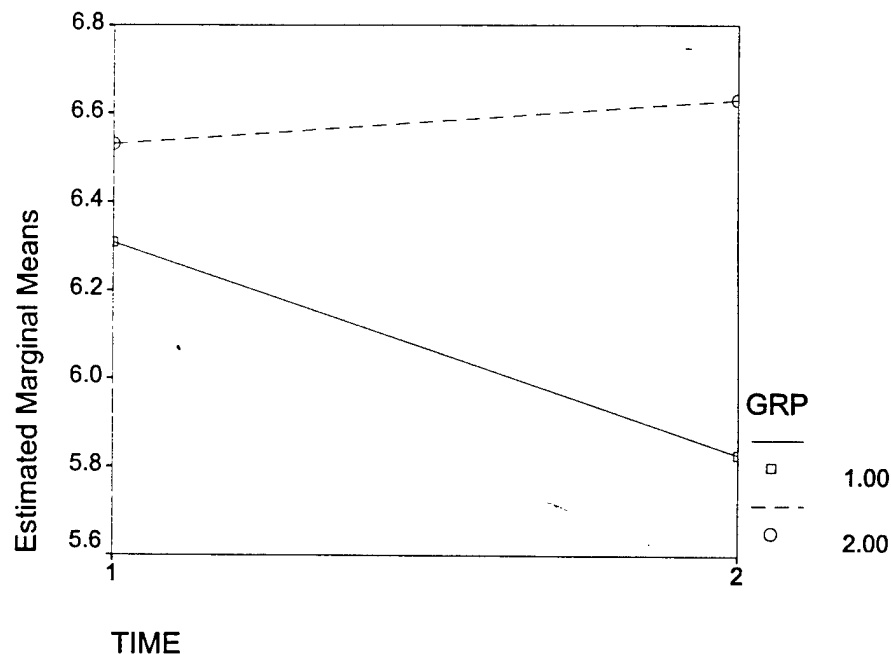
CAGRPS-Number of cancer groups belong to

PSSFA-Perceived support from family

PSSFR-Perceived support from friends

To test for significant group differences over time, 2 X 2 repeated measures anovas using the above variables as the outcome measure of interest were conducted. None of the analyses were significant at  $p < .05$ , all  $F$ 's  $\leq 3.03$ . Thus, at both the 4-month follow-up and the 12-month follow-up, the intervention group did not report significantly greater perceived social support or greater support availability. However, at the 4-month follow-up there were obvious trends in the SNI data indicating that the intervention participants reported increased SOC:  $F(1, 181) = 2.55$ ,  $p = .11$ ; GRPATT:  $F(1, 181) = 3.03$ ,  $p = .08$ ; and SNI:  $F(1, 181) = 2.66$ ,  $p = .10$  scores at the end of the intensive phase of the intervention in comparison to the control subjects who showed decreasing SNI total and subscale scores. This trend is illustrated below by the SNI total score data. In Figure 1, the dotted line represents the intervention arm and the solid line the assessment only arm. Time 1 = initial data point and Time 2 = 4-month follow-up.

Figure 1

SNI Scores Over Time By Group

**Hypothesis 2:** Do the intervention participants have significantly lower levels of cortisol than the assessment only subjects?

Again, repeated measures anovas (group by time) were used to test for significant group differences over time on the endocrine variables (CORT, ACTH, EPI, NEPI, HGH, PRL, and SCORT) were run. At the 4-month follow-up, the following endocrine variables were significant or showed trends indicating group differences over time:

Table 3

Significant Findings and Noteworthy Trends in the Endocrine Data

SCORT:  $F(1,19) = 2.05, p = .17$

CORT:  $F(1, 125) = 2.82, p = .09$

ACTH:  $F(1, 20) = 3.69, p = .07$

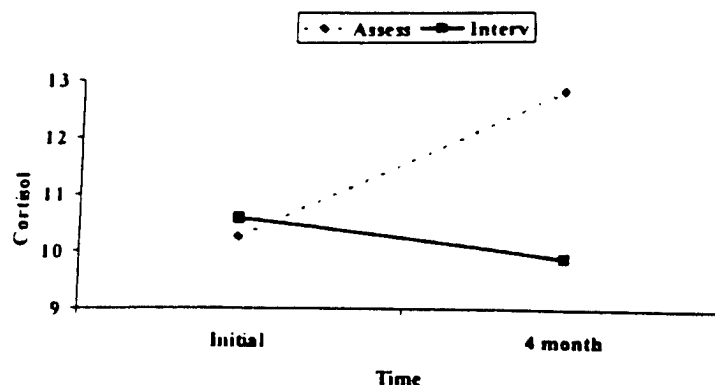
PRL:  $F(1, 92) = 3.92, p = .05$

NEPI:  $F(1, 36) = 8.37, p = .006$

The pattern of these group differences over time showed that the stress markers were decreasing for the intervention participants and increasing for the assessment only subjects. For illustrative purposes this pattern in the endocrine data is shown using the cortisol data in Figure 2. It should be noted that the repeated measures analyses resulted in some loss of data especially with the ACTH, SCORT, and NEPI variables. We are still in the process of converting endocrine data from the Malarkey lab as well as collecting data. Thus, over time these analyses will be repeated and any firm conclusions using these smaller sample sizes cannot be made at this time. None of the analyses conducted with the 12-month data were below  $p = .34$ .

Figure 2

Cortisol Changes By Group Over Time

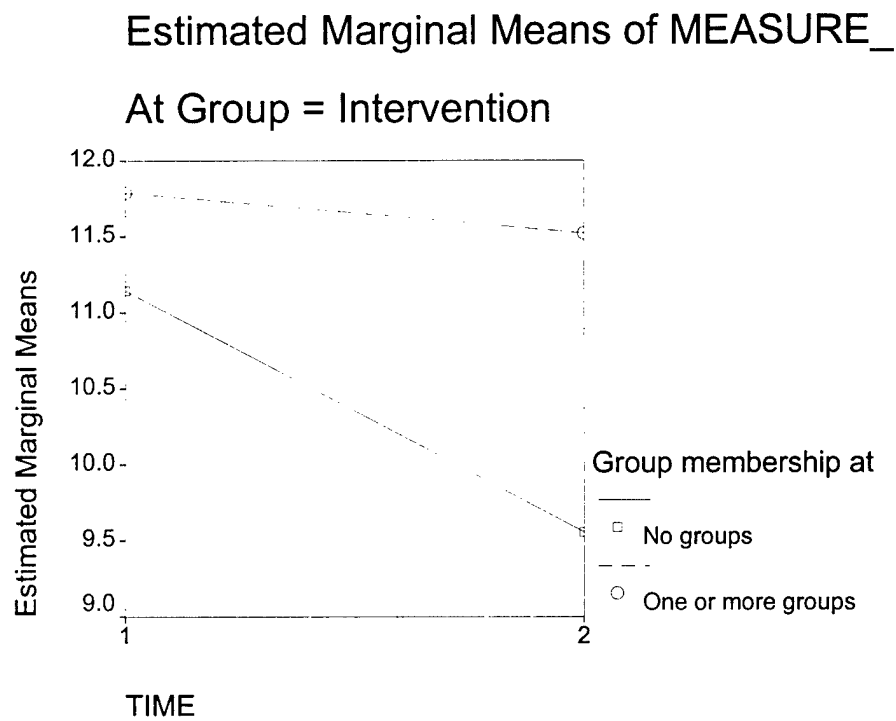
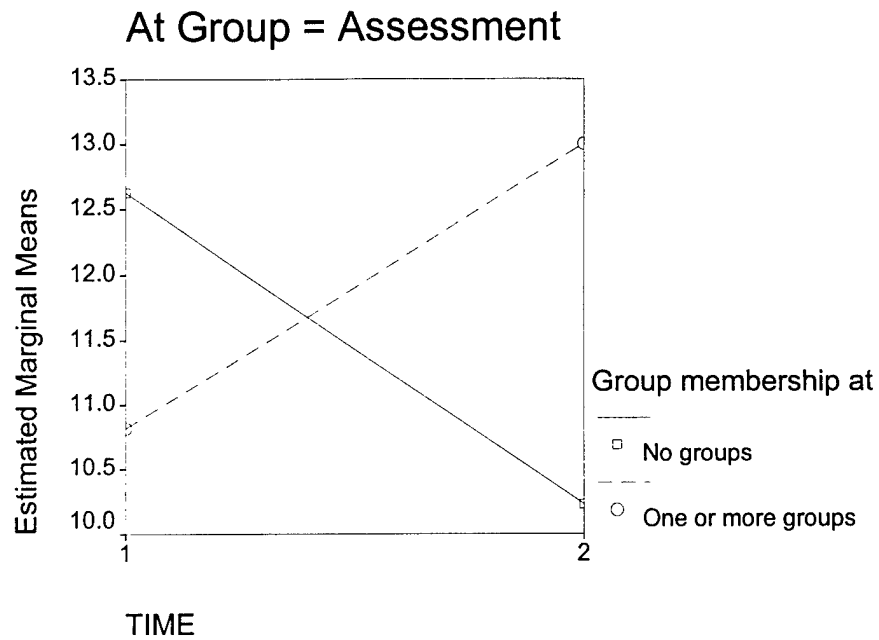


Furthermore, psychological stress and its relationship to depressive symptoms, the number one affective concern of cancer patients was examined. In particular, the relationship of objective stressors (life events) and subjective (perceived) stress to depressive symptoms were examined. Analyses controlled for alternative hypotheses including: sociodemographics, disease, and personality factors (neuroticism). Using Hierarchical Multiple Regression, 51% of the variance in depressive symptoms was predicted, accounted for by the control variables (race, neuroticism), objective stressors (major financial difficulty and major conflict were children/grandchildren), subjective event stress (cancer stress) and subjective global stress. An examination of the squared semipartial correlations indicated that perceived global stress (10%), cancer stress (8%), and race (1%) accounted for significant unique variance in the final model. These findings have been reviewed for publication in "Health Psychology" and we have been asked to submit the article as a brief report (Golden-Kreutz et al.). This work is included in the appendices. Please see Table 1 of the article. We have also shown that stress is also related to both emotional and physical quality of life and this work is now being prepared for publication. See Section 7: Reportable Outcomes for the reference and the appendices for a copy of the abstract.

**Hypothesis 3:** We wanted to test the stress buffering hypothesis of social support, that is test for an interaction between study arm (intervention vs. assessment only) and initial level of social support (high vs. low) across time (initial vs. post-treatment- 4-month follow-up) on endocrine function (e.g., cortisol). Again, we ran repeated measures anovas (group by time by social support variable) testing for changes in cortisol levels, our outcome of interest. Given sample sizes, the only endocrine variable tested at this time was CORT. When necessary we converted continuous social support data into categorical using median splits in order to conduct analyses (e.g., PSSFA, PSSFR, SNI, etc).

None of the analyses showed either significant three way interactions or two interactions,  $p < .05$ . In fact only one two-way interaction at the 4-month follow-up, time by GRPS, showed a trend towards significance,  $F(1, 122) = 3.43$ ,  $p = .07$ . This interaction is shown below: These effects are shown in the tables below. Thus, it appears that participation in the intervention results in a decrease in cortisol regardless of the number of groups belonged to although belonging to fewer groups is more likely to lead to a decrease in stress hormone levels. Meanwhile assessment only subjects who do not belong to other groups are more likely to show a decrease in cortisol levels than those assessment only subjects who belong to 1 or more groups. We will test the other endocrines for this effect as the data numbers increase.

Figure 3  
Interaction Data For Number of Groups Belong To By Study Arm



### Key Research Accomplishments

- *Golden-Kreutz, D., DeLamatre, M., Malarkey, W., & Andersen, B. (2000, June). The impact of a psychological/behavioral intervention on social support and endocrine function in women with breast cancer. **Invited Platform Presentation** and Poster presented at the Era of Hope Meeting sponsored by the Department of Defense Breast Cancer Research Program, Atlanta, Georgia.*
- *Golden-Kreutz, D., & Andersen, B. (Invited to submit as Brief Report). Correlates of depressive symptoms in women with regional breast cancer: Examining objective versus subjective stress after surgery. Health Psychology.*
- *Golden-Kreutz, D., Courtney, M., DiLillo, V., & Andersen, B. (2000, April). Objective stressors vs. subjective stress and their relationship to depressive symptoms: Examining the psychological responses to breast cancer diagnosis and treatment. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.*

## Reportable Outcomes

### **~~Manuscripts, abstracts, and presentations;~~**

#### ***Manuscripts:***

*Golden-Kreutz, D., Frierson, G., Brown, M., & Andersen, B. (Under review). Measurement invariance in longitudinal clinical research: Perceived stress in women with breast cancer. Psychological Assessment.*

*Golden-Kreutz, D., & Andersen, B. (Invited to submit as Brief Report). Correlates of depressive symptoms in women with regional breast cancer: Examining objective versus subjective stress after surgery. Health Psychology.*

*Andersen, B., Golden-Kreutz, D., McKolanis, J., Malarkey, W., Farrar, W., DeLamatre, M., & Finn, O. (Under review - Journal of National Cancer Institute). Recovery of tumor antigen (MUC1) specific antibody following successful stress reduction in breast cancer patients randomized to a psychological intervention in addition to standard therapy.*

*Andersen, B., Farrar, W., Golden-Kreutz, D., Kutz, L., MacCallum, R., Courtney, M.E., & Glaser, R. (1998). Stress alters immune responses following surgical treatment for regional breast cancer. Journal of National Cancer Institute, 90, 30-36.*

#### ***Presentations:***

*Golden-Kreutz, D., DeLamatre, M., Malarkey, W., & Andersen, B. (2000, June). The impact of a psychological/behavioral intervention on social support and endocrine function in women with breast cancer. Invited Platform Presentation and Poster presented at the Era of Hope Meeting sponsored by the Department of Defense Breast Cancer Research Program, Atlanta, Georgia.*

*Golden-Kreutz, D., Courtney, M., DiLillo, V., & Andersen, B. (2000, April). Objective stressors vs. subjective stress and their relationship to depressive symptoms: Examining the psychological responses to breast cancer diagnosis and treatment. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.*

*Frierson, G., Golden-Kreutz, D., Browne, M., & Andersen, B. (2000, April). The construct independence of perceived stress and depressive symptoms. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.*

*Pingel, K., Golden-Kreutz, D., Petri, M., & Andersen, B. (2000, April). Anxiety sensitivity: Its relationship to mood, social support, and somatic symptomatology in women post-adjuvant treatment for breast cancer. Poster presented at the Annual Meeting of the Society of Behavioral Medicine, Nashville, Tennessee.*

*Golden-Kreutz, D., Farrar, W., & Andersen, B. (1999, March). Conducting clinical research with breast cancer patients: Issues of recruitment and retention. Poster presented at the 2nd Annual meeting of "Women succeeding in Science in 1999: A Multidisciplinary Poster Session" sponsored by the Association for Women in Science of Central Ohio, The Ohio State University Office of Research, College of Biological Sciences and the Battelle Endowment for Technology and Human Affairs, Columbus, Ohio.*

*Golden-Kreutz, D., DiLillo, V., Farrar, W., & Andersen, B. (1998, July). The benefits of cognitive/behavioral interventions for women with breast cancer. World Congress of Behavioral and Cognitive Therapies, Acapulco, Mexico.*

***Book Chapters:***

Andersen, B., & *Golden-Kreutz, D.* (2000). Sexual-self concept for the woman with cancer: An Update. In L. Baider, C. Cooper, & A. Kaplan De-Nour (Eds.) *Cancer and the Family* (2nd ed), England: Wiley & Sons.

Andersen, B.L., *Golden-Kreutz, D.*, & DiLillo, V. (2000). Cancer, In A. E. Kazdin (Ed.), *Encyclopedia of Psychology*. Washington, DC: American Psychological Association Press.

Andersen, B.L., & *Golden-Kreutz, D.* & DiLillo, V. (1999). Cancer, In A. Baum, T. Revenson, & J. Singer (Eds.). *Handbook of Health Psychology*, NY: Erlbaum.

Andersen, B.L., & *Golden-Kreutz, D.* (1998). Cancer, In A.S. Bellack & M. Hersen (Eds.), *Comprehensive Clinical Psychology: Health Psychology (Vol.7)*, NY: Elsevier Science.

***Works in Progress:***

*Golden-Kreutz, D.*, Marlarkey, W., & Andersen, B. (prepare for publication). Social support and endocrine functioning in women with breast cancer.

*Golden-Kreutz, D.*, Thornton, L., Frierson, G., Lawrence, H., Wells, S., & Andersen, B. (prepare for publication). Negative changes in quality of life with the stress of cancer diagnosis and treatment.

**~~-Patents and licenses applied for and/or issued;~~** None

**~~-Degrees obtained that are supported by this award;~~** None

**~~-Development of cell lines, tissue or serum repositories;~~** None

**~~-Informatics such as databases and animal models, etc.;~~** None

**~~-Funding applied for based on work supported by this award;~~**

-NCI Grant with Barbara Andersen, PI, myself co-investigator

**~~-Employment or research opportunities applied for and/or received based on experiences/training supported by this award;~~**

-Opportunities to provide Continuing Education Units to other health professionals.

*Golden-Kreutz, D.* (2000, March). Use of psychological/behavioral interventions to reduce stress and enhance coping during breast cancer. Paper presented for the Student Nurses Association of Mt. Carmel Hospital and Mt Carmel Alumni Association Continuing Education Program (Nurses receive CEU credits for attending). Mount Carmel College of Nursing Lodge, Columbus, Ohio.



*Golden-Kreutz, D.* (1999, October). The Stress and Immunity Breast Cancer Project: Intervention effectiveness. Paper presented at a Mammography Seminar sponsored by the Central Ohio Society of Mammographers (Certified Mammographers receive CEU credits for attending), The James Cancer Hospital and Solove Research Institute, Columbus, Ohio.

-Asked to join a professional advisory board for Wellness Community and provide workshops to cancer patients and their families as well as staff.

*Golden-Kreutz, D.* (1999, October). Circle of supports. Workshop presented to cancer patients, family members, and staff at The Wellness Community, Columbus, Ohio. Workshop focused on ways of improving social support.

## Conclusions

This study on social support and endocrine functioning in stage II and III breast cancer patients randomized to either a psychological/behavioral intervention or a control arm found the following: (1) Over time, is an intervention associated with significantly higher levels of social support among the intervention subjects? Through this research effort, it was determined that breast cancer patients participating in an intervention do not report increased levels of social support over time compared to women who are in the control arm. However, it was found that at the end of the intensive phase of the intervention (e.g., weekly meetings for 4 months), a noteworthy trend existed in which intervention participants were reporting relatively stable social support while women in the control arm showed decreasing social support (Figure 1). It may be that social support, the way it is perceived by patients and its availability, with its long established patterns of dealing with family and friends are not easily or quickly changed, especially when dealing with a health crisis.

(2) Over time, is an intervention associated with significantly lower endocrine stress responses among intervention subjects? It was found that intervention participants do show decreased stress hormonal responses across a variety of endocrine hormones as compared to the control group at the 4-month follow-up (Figure 2). Thus, an intervention is associated with decreasing biological stress levels. This research result is important because it provides longitudinal data with a control group using several endocrine measures. Other research is needed to examine how hormone stress levels impact the immune system, especially for people with cancer. Thus, a psychological intervention may be able to boost/stabilize the immune system by altering stress hormone responses and this would have implications for survival. This is certainly a needed area of research.

(3) Test the stress buffering hypothesis of social support, that is test for an interaction between study arm (intervention vs. no intervention) and initial level of social support (high vs. low) across time (initial vs. post-treatment) on endocrine function (e.g., cortisol). In other words, do women with lower versus higher initial social support show different patterns of endocrine functioning over time based on whether they were assigned to the intervention or to the control arm of the study? It appears that participation in the intervention results in a decrease in cortisol regardless of the number of groups belonged to although belonging to fewer groups is more likely to lead to a decrease in stress hormone levels. Meanwhile assessment only subjects who do not belong to other groups are more likely to show a decrease in cortisol levels than those assessment only subjects who belong to 1 or more groups (Figure 3). This data does not support the notion of a buffering effect of social support. Rather it seems to indicate the reverse – those women who belong to more groups (which one may think would be associated with greater support) actually show increased stress hormone levels over time. It may well be that these group involvements are not supportive but rather represent commitments and may, in fact, be sources of additional stress given the women in the study are now also dealing with the diagnosis and treatment of breast cancer. This is further supported by the data showing that regardless of study arm, women who are not participating in groups, show lowered cortisol over time. This data is also supportive of the intervention's benefits. For example, the intervention was able to stabilize the cortisol level of those women belonging to other groups whereas the cortisol levels

of control women increase over time.

While significant findings and noteworthy trends in the data showing differences between the intervention and control arms of the study are available at the 4-month follow-up, no such results were found at the 12-month follow-up. It appears that many of the gains that the intervention women make during the intensive phase of the intervention are not maintained at 12-months with both groups looking essentially the same across the social support and endocrine variables. This appears to be largely due to the intervention going from weekly meetings to monthly meetings. Many women over the past several years have noted their disappointment when the groups meet less frequently and how much harder it is for them to stay focused on taking care of themselves (exercise, eating right, stress management). Thus, it may well be that psychological/behavioral intervention groups meeting less frequently are not able to effect/maintain positive effects for participants as well as groups meeting more frequently. This is an important point for researchers and agencies to consider when planning interventions. Furthermore, a psychological/behavioral intervention appears to be associated with more positive benefits for participants in comparison to other types of groups (e.g., recreational, professional, community). This may be especially true when a women is dealing with the cancer stressor and highlights the need for such groups.

NOTE:

- All publications and meeting abstracts related to this research effort are listed in Section 7: Reportable Outcomes.
- Only the PI of the study received pay from this research effort.

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Running head: DEPRESSIVE SYMPTOMS AND CANCER

Correlates of depressive symptoms in women with regional breast cancer:

Examining objective versus subjective stress after surgery

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Key words: Stress, depressive symptoms, breast cancer



## Abstract

The relationship of objective stressors (life events) and subjective (perceived) stress to depressive symptoms was examined. These relationships were explored in stressed individuals, potentially vulnerable to the experience of depressive symptoms, namely 210 women recently diagnosed and surgically treated for regional (stage II or III) breast cancer. Analyses controlled for potentially relevant correlates including sociodemographic, disease, and personality factors. Using Hierarchical Multiple Regression, 53% of the variance in depressive symptoms was accounted for by the control variables (race and neuroticism), an objective stressor (major financial difficulty), and perceptions of cancer stress (IES) and global stress (PSS-10). These findings provide needed information regarding the correlates of depressive symptoms in women with regional breast cancer for whom the risk of recurrence is significant.

## Correlates of depressive symptoms in women with regional breast cancer:

## Examining objective versus subjective stress after surgery

It has been suggested that half of all cancer patients will meet the American Psychiatric Association's criteria for a psychiatric diagnosis (e.g., depressive, anxiety, or adjustment disorder; e.g., Derogatis et al., 1983; Spiegel, 1996). In fact, depressive symptoms are the most common affective symptoms reported by this population (See Tope, Ahles, & Silverfarb, 1993, and van't Spiker, Trijsburg, & Duivenvoorden, 1997 for reviews). Breast cancer alone, the most commonly diagnosed cancer in women, annually yields over 182,000 new cases in the United States (Greenlee, Murray, Bolden, & Wingo, 2000). Thus, upwards of 91,000 women will experience some level of depressive symptoms and some subset of these will actually have depressive symptoms of clinical significance (e.g., depression). While reports of depression in women with breast cancer have ranged from 0% (Greenberg, Sawicka, Eisenthal, & Ross, 1992) to 57% (Sachs et al., 1995), more typical are rates of 20-30% (e.g., Fallowfield, Hall, Maguire, & Baum, 1990; Goldberg et al., 1992; Rijken, deKruif, Komproe, & Roussell, 1995). Because much of this previous research has been conducted with patients diagnosed with either local (stage 0 or I; e.g., Greenberg et al., 1992; Sachs et al., 1995; Rijken et al., 1995) or recurrent disease (e.g., Jenkins, May & Hughes, 1991; Pinder et al., 1993), little is known about depressive symptoms in women at moderate risk, that is, women with regional disease (i.e., stage II or III). This is important as extent (i.e., stage) of disease at diagnosis has routinely been associated with more emotional distress including depressive symptoms/depression (e.g., Glanz & Lerman, 1992; Desai, Bruce, & Kasl, 1999; Pinder et al., 1993; Stanton & Snider, 1993). Therefore, we were interested in identifying correlates of depressive symptoms in women with regional breast cancer. In addition to the trauma of diagnosis, there is the added worry and concern about prognosis as the risk for recurrence is higher for this group. For example, 10 year survival

estimates are 66% for stage II and 36% for stage III. This is in contrast to 95%, 88%, and 7% survival rates for stages 0, I, and IV, respectively (Fremgen et al., 1999). In this context, we were interested in examining the association of objective (life events) and subjective (perceived) stress to depressive symptoms.

#### The association of objective and subjective stress to psychological distress

Stress, whether measured objectively (as life events) or subjectively (as perceptions), is associated with poor psychological and physical outcomes across a variety of groups (e.g., college students and adults in community smoking cessation program: Cohen, Kamarck, & Mermelstein, 1983; adult psychiatric patients: Hewitt, Flett, & Mosher, 1992; highway patrol officers: Hills & Norvell, 1991). That the diagnosis and treatment of cancer are significant life stressors with a negative impact on psychological well-being, quality of life, and health has been thoroughly discussed (e.g., Andersen, Kiecolt-Glaser, & Glaser, 1994; Spiegel, 1996). While studies may include both objective and subjective measures of stress, few studies have examined their relative associations to other psychological variables (e.g., depressive symptoms; Cohen et al., 1983; Cohen & Williamson, 1988; Hills & Norvell, 1991; Pbert, Doerfler, & DeCosimo, 1992), and studies with cancer samples are rare.

#### Objective stressors (life events)

Studies have examined life events as predictors of cancer risk (e.g., Ginsberg, Price, Ingram, & Nottage, 1996; Protheroe et al., 1999; Roberts, Newcomb, Trentham-Dietz, & Storer, 1996). In fact, a recent meta-analysis (McKenna, Zevon, Corn, & Rounds, 1999) examining psychosocial factors and the development of breast cancer found significant effect sizes for denial/repression coping, separation/loss experiences (defined as the experience of any type of loss of a close emotional relationship), and stressful life events (not specifically identified). Mazure (1998) has stated that compelling evidence exists for the association between adverse

life events and subsequent depression, specifically major depression, yet few studies have examined the relationship between life events and the distress of cancer diagnosis and treatment.

Some data do suggest that an increased number of recent life events are positively related to distress (Bukberg, Penman, & Holland, 1984; Grassi, Malacarne, Maestri, & Ramelli, 1997; & VanServellen, Sarna, Padilla, & Brecht, 1996).

#### Subjective stress (perceptions)

While early cancer studies documented acute distress experienced at diagnosis (e.g., Andersen, Anderson, & deProse, 1989; Weisman & Worden, 1976), contemporary studies suggest that cancer diagnosis and treatment may, in fact, constitute a "traumatic event" (4th ed; DSM-IV: American Psychiatric Association, 1994; Cordova et al., 1995; Andrykowski, Cordova, Miller, & Studts, 1998). As a result, existing measures of traumatic stress such as the Impact of Events Scale (IES; Horowitz, Wilner, & Alvarez, 1979) have been modified for cancer populations (changing the word "event" on the original scale to "disease" or "cancer"). Much of the research examining cancer stress has, in fact, used the IES to examine the frequency or severity of trauma-related intrusive cognitions and avoidant behaviors, and their relationships to psychological outcomes (Baider & De-Nour, 1997; Cordova et al., 1995; Schwartz, Lerman, Miller, Daly, & Masny, 1995). There are consistent, positive relationships between intrusive thoughts and severity of psychological distress (e.g., patients at high risk for cancer, Schwartz et al., 1995), and weak, if any, relationships between avoidant thoughts/behaviors and psychological distress (for breast cancer patients, see Baider & De-Nour, 1997 or Cordova et al., 1995; for parents of pediatric cancer patients, see Hall & Baum, 1995).

In contrast to the common use of subjective ratings of the cancer "event," few cancer studies include globally perceived stress measures. One exception is a study by Varni and colleagues (1994) who found that higher perceived global stress predicted increased

psychological distress (e.g., depression and anxiety) in adolescent survivors of pediatric cancer (see also Bull & Drotar, 1991 or Schulz et al., 1995 for other examples). In comparing these three strategies of measuring stress, researchers have typically employed objective stress measures or subjective ratings of the cancer experience, with fewer studies examining subjective global stress.

#### Correlates of depressive symptoms in women with breast cancer

Sociodemographic, disease, and personality characteristics have been linked to depressive symptoms in women with breast cancer. Sociodemographic variables (e.g., age, race, SES) are correlated with breast cancer incidence and/or mortality (Faggiano, Partanen, Kogevinas, & Boffetta, 1997; Landis et al., 1999; Schrijvers & Mackenback, 1994), but their relationship to depressive symptoms is inconclusive (Carver et al., 1994; Dean, 1987; Hughson, Cooper, McArdle, & Smith, 1988; Lee et al. 1992; Levy et al., 1992; Pinder et al., 1993; Stanton & Snider, 1993). Disease variables such as stage of disease, extent of surgical treatment, and time since diagnosis/treatment are related, in general, to psychological outcomes in women with breast cancer. In particular, data suggest that women with more advanced disease may have more severe depressive symptoms (e.g., Glanz & Lerman, 1992; Desai et al., 1999; Pinder et al., 1993; Stanton & Snider, 1993). Personality variables, most commonly neuroticism, have also been examined. While positive associations between neuroticism and negative affective states (e.g., depressive symptoms) have been found in heterogeneous cancer groups (Jenkins et al., 1991; VanderZee, Buunk, & Sanderman, 1996), the specificity with regards to breast cancer patients needs to be investigated. This potential relationship may be particularly important as neuroticism is consistently associated with psychological distress in other non-cancer populations (e.g., Clark, Watson, & Minneka, 1994; Watson, 1988), and has been proposed as a risk factor for psychological distress (Clark et al., 1994; Watson & Pennebaker, 1989).

Additional research is needed in order to clarify the relationship of these variables to depressive symptoms.

### Aim of the research

In the present study, the relationship of objective stressors and subjective stress to depressive symptoms in women with regional breast cancer is examined after variables associated with these symptoms were controlled. We are focusing on women with regional disease as there has been little systematic research on this breast cancer group and we anticipated that both stress and depressive symptoms might be prevalent in this group. Specifically, we were interested in testing the relationship of life events and perceived stress (both stress perceptions specific to cancer and more global ones) to depressive symptoms. In particular, we are focusing on identifying those life events (e.g., death of loved) associated with depressive symptoms. Further, we wanted to explore the relative contributions of life event stress versus perceptions of cancer stress and global stress to the severity of depressive symptoms. Finally, to highlight the contribution of stress we controlled for those variables (sociodemographics, disease characteristics, and neuroticism) which may be correlated to depressive symptoms, per se.

### Method

#### Participants

Participants were 210 women who had been diagnosed with Stage II (89%) or III (11%) breast cancer. All of the participants had been surgically treated (lumpectomy = 41%; mastectomy = 59%) within the preceding 3 months (days since surgery:  $\underline{M}$  = 36.20;  $\underline{SD}$  = 16.89). Sociodemographic description of the sample was as follows: age ( $\underline{M}$  = 51.02 years,  $\underline{SD}$  = 10.83), racial group (White = 90%; African American = 9%; Hispanic = 1%), and partner status (72% with a partner). The distribution of the total years of education was <12 years = 4%; 12 years = 25%; 13-15 years = 28%; 16 years = 18%; and >16 years = 25%. Distribution of annual family

income was <\$15,000 = 9%; \$15-29,000 = 16%; \$30-49,000 = 23%; \$50-79,000 = 24%; and ≥\$80,000 = 28%. Eleven women declined to give information about income.

### Procedures

Participants were accrued from 1994 to 1999 for a larger prospective, longitudinal study (The Stress and Immunity Breast Cancer Project).<sup>1</sup> The women were recruited primarily from physician's offices at a National Cancer Institute-designated university-affiliated Comprehensive Cancer Center (82%). Other participants were self referrals from newspaper advertisements, press releases, and project flyers (18%). Participation refusal rates are 30%. The most frequent reasons for declining participation were distance (too far to travel from home to the university) and lack of time or interest. All women were assessed after surgery and prior to beginning adjuvant treatment (e.g., chemotherapy, radiation). Psychological, behavioral, and medical/treatment information were collected with an interview and questionnaires. Assessments were conducted at the University's General Clinical Research Center or the breast cancer clinic. Disease and surgery information were verified using information from the women's medical charts/reports and confirmed with primary care providers. All women were paid \$20.00 for their participation.

### Measures

#### Control variables

Sociodemographics, disease characteristics, and personality. Three classes of variables were considered for possible control in the data analyses to follow. The sociodemographic variables included: age, race (White vs. minority status), partner status (yes vs. no), education (years), and family income (dollars per year). The disease variables examined were stage of disease (stage II vs. stage III), extent of surgery (lumpectomy vs. mastectomy), and time since surgery (in days). Disease staging was based on the American Joint Committee on Cancer and

the International Union Against Cancer staging systems. Days since surgery was calculated as the number of days between surgery and the initial assessment.

The personality variable included was neuroticism, as assessed with Goldberg's Big-Five Factor Measure (1992). The items as originally suggested by Goldberg (1992) were used following a confirmatory factor analysis. Neuroticism was assessed using 15 trait adjectives, 9 scored in the positive direction (e.g., irritable, nervous) and 6 scored in the negative direction (e.g., even-tempered, at-ease). Each woman rated the extent to which these trait adjectives described her, as compared to others of the same sex and age, on a nine-point Likert scale from "extremely inaccurate" (9) to "extremely accurately" (0). Total scores can range from -63 to 81, with higher scores indicating stronger trait neuroticism. In the present study, the average neuroticism score of the participants was .49 ( $SD = 17.66$ ; range -36 to 68) and the coefficient alpha reliability was .90.

#### Stress measures

Objective stressors (life events). The event scale used was adapted from that in the Women's Health Initiative study (Matthews et al., 1997). Participants were asked to indicate if they had experienced any of five stressful life events, previously identified as being stressful for women. These events were 1) death or serious illness of a close friend or relative, 2) major financial difficulty, 3) divorce or other breakup involving family members (spouse) or close friends, 4) major conflict with children or grandchildren, and 5) muggings, robberies, accidents, or similar events. By assessing the occurrence of life events over the previous year, the chronic or long-term impact of life events on later adjustment is assessed. If an event occurred, women then rated how emotionally upsetting the event was (3=very much, 2=moderately, 1=not much). Three scores were calculated: presence versus absence of each event (0=not occurred, 1=occurred), the distress rating for each event (given above), and the total number of events



reported (range 0-5).

Subjective cancer stress. The IES (Horowitz et al., 1979) is a standardized self-report measure used to examine cognitions involving the re-experiencing (intrusion) and denial of thoughts and avoidant behaviors (avoidance) related to trauma (Miller, 1996). Fifteen items are used, seven for the intrusive subscale (e.g., "I had trouble falling or staying asleep because pictures or thoughts about cancer or having cancer treatment came into my mind") and eight items for the avoidant subscale (e.g., "I tried not to think about it"). Consistent with previous research, the word "event" was changed to "cancer." Women rated each item as experienced in the previous week, using a 4-point Likert scale (not at all=0, rarely=1, sometimes=3, and often=5). Three scores are obtained from the IES, a total score (IES-T) and intrusion (IES-I) and avoidance (IES-A) subscale scores. Total scores can range from 0 to 75 with higher scores indicating increased severity of cancer-related stress. Intrusion and avoidance subscales range from 0 to 35 and 0 to 40, respectively. In the present sample the coefficient alpha reliability was .83, consistent with other studies reporting reliabilities of .78-.83 (Cordova et al. 1995, Horowitz et al., 1979; Schwartz et al., 1995).

Subjective global stress. The Perceived Stress Scale (PSS; Cohen et al., 1983), a measure of perceived stress, is a standardized self-report questionnaire used to determine the extent to which a person judges her/his life to be unpredictable, uncontrollable, and overloading (Cohen et al., 1983). Based on Cohen and Williamson's (1988) recommendation, the ten item PSS-10 was used for its improved internal reliability and factor structure over other versions of the PSS. Examples of the questions include: "How often have you felt nervous or stressed" and "How often have you felt confident about your ability to handle your personal problems." Women rated how often they experienced the above feelings in the past month on a 5-point Likert scale (from never=1 to very often=5). Total scores range from 0 to 40 and higher scores indicate

greater overall stress. Coefficient alpha reliability was .87 in the present sample and ranges from .75 to .86 in the literature (Cohen et al., 1983; Hewitt et al., 1992; Martin, Kazarian, & Breiter, 1995; & Pbert et al., 1992).

### Outcome

Depressive symptoms. The short form (IOWA version, Kohout, Berkman, Evans, & Cornoni-Huntley, 1993) of the Center for Epidemiological Studies Depression scale (CES-D; Comstock & Helsing, 1976; Radloff, 1977) is a standardized self-report questionnaire used to identify current symptoms of depression, with emphasis on depressed affect. The CES-D short form consists of 11 items (e.g., "I felt everything I did was an effort" and "I felt sad") rated on a 3-point Likert scale from "hardly ever or never=0" to "much or most of the time=2."

Participants were asked to respond based on their feelings during the previous week. Total scores range from 0 to 22 with higher scores reflecting greater depressive symptoms. Unlike other measures of depressive symptoms (e.g., Beck Depression Inventory, Hamilton Rating Scale for Depression), the CES-D is relatively unaffected by physical symptoms and is, therefore, commonly used in research with medical patients (Devins et al., 1988). Further, the CES-D has been established as a valid and reliable measure of depressive symptoms in women with breast cancer (Hann, Winter, & Jacobsen, 1999). Coefficient alpha reliability in the present sample was .77, consistent with other research (Himmelfarb & Murell, 1983; Kohout et al., 1993).

### Analytic approach

Correlations were used to test the significance and direction of association between the control variables, stress measures, and depressive symptoms. Pearson bivariate correlations were calculated among continuous variables and Spearman rank-order correlations were calculated when one variable was categorical and the other was continuous. Next, hierarchical

multiple regression (HMR) analyses along with squared semi-partial were used to examine how the control variables and stress measures were related to depressive symptomatology. Variables significantly correlated with depressive symptoms were tested in the regression analyses.

Variable entry was determined by a priori theoretical and empirical rationale. Specifically, when the differential predictive power of objective versus subjective measures have been compared, subjective measures have consistently been stronger predictors of psychological and physical outcomes (Cohen et al., 1983; Martin et al., 1995; Pbert et al., 1992; Sarason, Johnson, & Siegel, 1978; Vinokur & Selzer, 1975). Further, research has suggested that global subjective stress ratings may be a stronger predictor of psychological outcomes than either objective or event specific measures of stressors (Cohen et al., 1983; Kuiper, Olinger, & Lyons, 1986; Martin et al., 1995; Pbert et al., 1992). Therefore, variable entry was as follows: control variables (sociodemographics, neuroticism, and disease characteristics), life events, cancer stress, and finally, global stress.

## Results

### Preliminary analyses

#### Descriptive data

Stress measures. The majority (74%) of participants experienced at least one major life event in the year prior to their breast cancer diagnosis (0 events = 26%; 1 event = 41%; 2 events = 18%; 3 events = 10%; 4 events = 4%; and 5 events = 1%). The modal subjective stress associated with an event was rated as 3.0=very much upsetting. The most common event reported was the death or serious illness of a relative or close friend (50%, n = 104) followed by major financial difficulty (24%, n = 51), divorce or breakup involving family members/close friends (20%, n = 41), major conflict with children/grandchildren (18%, n = 38), and muggings, robberies, accidents or similar events (12%, n = 32).

The mean of the IES-T was 25.23 ( $SD = 14.06$ , range 0-65), a value at least  $\frac{1}{2}$  SD higher than those reported in other breast cancer samples ( $M = 16.4$ , Cordova et al., 1995;  $M = 11.5$ , Baider, Peretz, & De-Nour, 1992). According to the scale authors, total scores above 19 are considered clinically significant in that feelings/behaviors are at a problematic level (Horowitz, Field, & Classen, 1993). Avoidance and Intrusion subscale means were 12.41 ( $SD = 7.78$ , range 0-36) and 12.81 ( $SD = 8.29$ , range 0-35), respectively. The average PSS-10 score was 18.32 ( $SD = 6.96$ , range 1-36), a value nearing 1 SD higher than the mean score from a national probability sample of adults ( $M = 13.02$ ; Cohen and Williamson, 1988). In summary, the data suggest that the participants were reporting psychological stress across both objective and subjective measures.

Depressive symptoms. CES-D scores ranged from 0 to 18 with a sample mean of 5.96 ( $SD = 3.67$ ). Based on previous psychometric studies of the CES-D (Andresen, Malmgren, Carter, & Patrick, 1994), a cut-off score of  $\geq 10$  is considered suggestive of clinical depression. In the current study, a score of 10 was 1 SD above the sample mean. Eighteen percent ( $n = 38$ ) of the participants had CES-D scores meeting/exceeding the cut-off. An additional 9% ( $n = 18$ ) of the women had the score of 9, one point below the cut-off score. In all, one fifth of the women may have been experiencing depressive symptoms of possible clinical importance (i.e., scores  $\geq 10$ ). This is comparable to rates of depressive symptoms found in previous studies of women with breast cancer (e.g., Rijken et al., 1995; Watson et al., 1991).

### Primary analyses

#### Correlations

Of the nine control variables tested (age, race, partner status, education, family income, stage of disease, extent of surgery, days since surgery, and neuroticism), only two were significantly correlated with depressive symptoms, race ( $r = .17$ ,  $p < .02$ ) and neuroticism

( $r = .44$ ,  $p < .0001$ ). Thus, being of minority status (i.e., African American or Hispanic) or having higher levels of neuroticism were related to higher CES-D scores. Based on these results, race and neuroticism were included in the regression analyses.

We also examined the correlations among the objective stressors, subjective stress measures, and depressive symptoms. Specifically, only the life event of "major financial difficulty" was significantly correlated with CES-D scores at  $p \leq .05$  ( $r = .25$ ). The IES-T, its subscales, and the PSS-10 were also significantly correlated with CES-D scores at  $p \leq .05$ . As the shared variance between the PSS-10 and the CES-D was noteworthy ( $r = .65$ ; 42%), it was important to rule out the possibility of measure overlap at the item level. Results of a factor analysis verified no overlap of item content between measures (Frierson, Golden-Kreutz, Browne, & Andersen, 2000).<sup>2</sup> Thus, the results described below are not confounded by shared item/content variance between the PSS-10 and CES-D.

### Regression

HMR was used to examine the relationships among the objective stressor (major financial difficulty), subjective cancer stress (IES), and subjective global stress (PSS-10) to depressive symptoms after controlling for the effects of race and neuroticism. The a priori entry was as follows: Step 1) the control variables: race and neuroticism, 2) the life event: major financial difficulty, 3) cancer stress: IES-T, and 4) global stress: PSS-10.

Table 1 shows results for the final regression model. The model was significant,  $F(5, 209) = 45.84$ ,  $p < .0001$ . Moreover, fifty-three percent of the variance (total adjusted  $R^2 = .518$ ) in depressive symptoms was accounted for by the hypothesized predictors. The contribution of the control factors accounted for 20% of the variance, whereas the addition of the objective and perceived stress measurements accounted for the larger portion of the total, 33%. Entered in the order of objective stressors (life events), cancer stress, and global stress, the

stress measures accounted for the following increments in total variance: 4%, 18%, and 10%, respectively. As a follow-up to these significant results, we also calculated for each variable in the equation the squared semi-partial correlation,  $sr^2$ . These correlations indicate the amount of variance accounted for by a given variable above and beyond all other variables in the regression model (i.e., the amount of variance accounted for by the variable if it been entered last in the regression equation, Cohen & Cohen, 1983). For the stress variables, the strongest correlate of depressive symptoms was global stress (11%), followed by cancer stress (5%), and then the objective stressor-major financial difficulty (2%). The control variables, neuroticism and race, each accounted for approximately 1% of the variance in the regression model.

#### Follow-up analyses

Because of the empirical and clinical importance of the cancer stress measure, we wished to test the relative contribution of avoidance versus intrusive thoughts/behaviors to depressive symptoms. Therefore, a second regression was conducted using the IES subscales, IES-A and IES-I, in place of the IES-T. Variables were entered as before: Step 1) race and neuroticism, 2) major financial difficulty, 3) IES-A, 4) IES-I, and 5) PSS-10. Based on past research, IES-A was entered before IES-I because of its weaker relationship with psychological outcomes (e.g., Baider & De-Nour, 1997; Cordova et al., 1995). Results from this follow-up analysis indicate that, 54% of the variance (total adjusted  $R^2 = .527$ ) in depressive symptoms was accounted for by the HMR,  $F(6, 209) = 39.83$ ,  $p < .0001$ . Specifically, the IES-A did not contribute a significant increment of unique variance to the final model ( $\beta = .045$ ;  $t < 1.00$ ;  $sr^2 = .005$ ) whereas the IES-I did ( $\beta = .285$ ;  $t = 4.51$ ;  $sr^2 = .05$ ). This finding is consistent with previous literature (e.g., Baider & De-Nour, 1997; Cordova et al., 1995) showing zero or weak relationships between avoidant thoughts/behaviors and psychological distress. As before, all of the remaining variables were significantly associated ( $p < .05$ ) with depressive symptoms in the final regression

model. The amount of variance accounted for, again using  $sr^2$  values, was 9% (PSS-10), 5% (IES-I), 2% (major financial difficulty), and 1% (each for neuroticism and race).

### Discussion

The present study examined the relationship of objective stressors and subjective stress to depressive symptoms in women after receiving surgery for regional breast cancer. The relationships were explored after variables associated with these symptoms were controlled (sociodemographics, disease characteristics, and neuroticism). We identified the following variables as significant correlates of depressive symptoms: 1) the control variables: race (minority status) and neuroticism, 2) the life event: major financial difficulty, 3) perceived stress related to cancer (specifically stress manifest by intrusive thoughts), and 4) perceptions of global stress. More particularly, we found that global perceptions of stress were stronger correlates of depressive symptoms than either perceptions of stress specific to the cancer experience or stress with life events.

We examined variables such as sociodemographics (age, race, partner status, education, and family income) and personality (neuroticism), all of which are known to correlate with depressive symptoms. In addition to personality and sociodemographic variables, we also chose ones relevant for the present paradigm--disease characteristics (e.g., stage of disease, extent of surgery, days since surgery). Of all these variables, only neuroticism and race (minority status) were significantly related to depressive symptoms in the final model of the HMR. While previous studies find links between psychological outcomes and neuroticism in heterogeneous cancer groups (Jenkins et al., 1991; VanderZee et al., 1996), this study confirms this association in women with breast cancer. These data suggest that the trait of neuroticism may heighten risk for depressive symptoms in women with breast cancer. These data also suggest that minority status is associated with more depressive symptoms. As the number of minority participants in

the present study was small ( $n = 22$ , 10% of the total sample), this finding will require replication with a larger minority sample before a general conclusion can be made. Besides socio-economic differences, it is also possible that this finding is related to other variables associated with race/ethnicity and cancer outcomes, such as knowledge and attitudes and/or access to adequate care (see Meyerowitz, Richardson, Hudson, & Leedham, 1998, for a review).

While half of the participants reported experiencing the death or serious illness of a close friend or relative in the previous 12 months (a fact not surprising considering the age range of the sample), it was "major financial difficulty" that was a significant correlate of depressive symptoms in the HMR model ( $p < .01$ ). We do not know if this life event represents a chronic or recent stressor as the time frame for these items was "the last 12 months." Research has indicated that the cancer experience can have subsequent detrimental consequences on finances (e.g., loss of income due to work absences, increased insurance costs; McKenna, 1991; McKenna & Toghia, 1989). For our participants, however, these cancer specific effects may not have accumulated as they were in the earliest stages of their illness/treatment (i.e., 36 mean days since surgery,  $SD = 17$ ). Nevertheless, if we consider this finding in the context of other important information, 28% of all U.S. households are headed by unmarried women and 57% of all women work outside the home (U.S. Bureau of the Census, 1995; 1996). In particular, the stressor of "major financial difficulty" may, unfortunately, be a common one for a subset of the thousands of women diagnosed with breast cancer each year (e.g., over 182,000 in 2000; Greenlee et al., 2000).

Further consequences of financial difficulties may include: the selection of medical therapies (e.g., absence of insurance coverage for treatments), the delay of medical treatment due to employment conflicts, transportation difficulties (e.g., not owning a car), and decrease overall quality of life. Therefore, the data suggest that financial stressors and their potential negative



impact on the already stressful experience of a cancer diagnosis may increase one's vulnerability to depressive symptoms. Health care providers may want to be particularly aware of those women who are struggling financially. Linking women with appropriate psychological, social, and/or financial services to meet these needs may be important.

A global perception of stress, as assessed with the PSS-10, was the strongest correlate of depressive symptoms. This finding is impressive considering the clinical importance of the event -- cancer diagnosis, surgical treatment, and the anticipation of further treatment/s (e.g., chemotherapy, radiation, hormone therapy). A testimony to the significance of the cancer experience was from the study participants themselves, as many women subsequently related that they were enrolled into the study and assessed on "the worst days of my life." Such a characterization is consistent with the IES follow-up analysis indicating intrusive thoughts rather than avoidance were a stronger correlate of depressive symptoms. Finally, the mean values on the PSS-10 and IES were, at a minimum, one-half to one standard deviation higher than values with data from other cancer or normative samples. Thus, many of the women were stressed not only by their cancer experience but with life, in general. These data are consistent with others examining the relationship between stress and psychological outcomes (e.g., Cohen et al., 1983) and underscore the importance of perceptions or appraisals of stress (instead of or in addition to the assessment of events, *per se*). The value of assessing both objective stressors and subjective stress (event specific and global) is important as such information can increase our understanding of how life events and stress perceptions are related to psychological functioning as well as identify circumstances in which people may be in need of intervention.

Considering the  $sr^2$  data, the relative contribution of the objective stress measure (2% for major financial difficulty) was smaller than that for the subjective measures (11% for the PSS-10 and 5% for the IES). There may be several factors contributing to this differential. For example,

the contribution of stressful events may be smaller because their impact may have lessened with time. These events occurred at some point in the past 12 months, and stress from them may have resolved by the time of assessment. Meanwhile, the time from cancer diagnosis to post surgery recovery and study participation was, on average, 4 weeks. Using the standard administration procedures for these measures may have confounded the rating interval with the measure (e.g., past 12 months for the objective stressors vs. past month for global stress and past week for cancer specific stress). This likely has a statistical effect on the magnitude of the correlation between the measures and the outcome. In this case, the relationship between the subjective stress measures and the outcome would be expected to be higher because of the shorter and more proximal rating interval. Another methodological difference between the measures is the item format. That is, measures assessing the degree of distress associated with life events typically use only one item per event, which reduces the reliability of the measure. This contrasts with the multiple item format of the IES or PSS-10. Taken together, these methodologic aspects of objective stress measures may contribute to the findings reported here, as well as those of other investigators who have reported that event measures are, on average, weaker predictors in comparison to subjective global stress measures (Cohen et al., 1983; Martin et al., 1995; Pbert et al., 1992), even when some of the objective events rated are the most difficult ones individual's can experience (e.g., death of a loved one). Given the design of the current study, no causal inferences can be made. However, future research can examine the reliability of these relationships longitudinally, establish causal explanations, and test their generalizability with other cancer groups.

In summary, these findings provide an important look at the emotional crisis that surrounds cancer diagnosis and surgery in women with regional breast cancer. Obtaining a large homogeneous sample in terms of extent of disease and prognosis and controlling the timing of

the assessment to occur at a maximally stressful point were important research design features in exploring these questions. Our earlier research on the emotional responses to cancer diagnosis with a sample that was diagnostically more varied (i.e., stages I, II, or III gynecologic cancers; Andersen et al., 1989) but assessed at the same difficult time point found that depressive and confused moods were unique emotional responses for women with cancer. Anxious reactions were common as well, but were likely part of the general emotional response to a medical diagnosis and the anticipation of medical treatment, rather than cancer, *per se*. More recently, we have reported that cancer specific stress (as indexed by the IES) is not only emotionally upsetting, but is related to a negative biologic response -- immune down regulation (Andersen et al., 1998), and we have hypothesized that such a scenario may adversely impact the course of the disease (Andersen et al., 1994). These data indicate that the stress indexed by the IES, coupled with the global feelings of stress and recent life event stressors, may conspire to heighten one's risk for depressive symptomatology. In reviewing the literature on psychosocial interventions (Andersen, 1992), we noted that stress reduction is a component of successful interventions. Considering these data along with our other studies, they suggest that stress reduction should be included to not only lower stress and anxiety, but to lower risk for other negative affective symptoms (e.g., depressive ones) which may, in turn, have important biologic effects (Herbert & Cohen, 1993).

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## Author Note

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## Footnotes

<sup>1</sup> The Stress and Immunity Breast Cancer Project is an ongoing study conducted at the Department of Psychology in collaboration with the James Cancer Hospital and Research Institute, at The Ohio State University, Columbus, Ohio. Data from the first 116 women accrued to the Stress and Immunity Breast Cancer Project (including 116 of the 210 women included here) have appeared in a report of the negative relationship between stress (as indexed by the IES) and multiple immune indicators (Andersen et al., 1998). Aside from the IES, there is no overlap of measures between Andersen et al. (1998) and the present report.

<sup>2</sup>We conducted a PACE factor analysis using the program CEFA (Browne, Cudeck, Tateneni, & Mels, 1998). According to previous research, the short form of the CES-D has 4 factors (1-depressed affect; 2-positive affect; 3-somatic complaints, and 4-interpersonal problems; Kohout et al., 1993) while the PSS-10 has 2 identified factors (1-distress; 2-coping; Cohen & Williamson, 1988; Hewitt et al., 1992; Martin et al., 1995). We combined the PSS-10 and CES-D ( $n = 166$ ), and oblique rotation to a partially specified target (Browne, 1972) was carried out to test the factor loadings for construct redundancy. Loadings anticipated to be zero were minimized in the rotation process and values of the remaining loadings were left unspecified. Thus a pattern suggested by current research (6 factors) was tested and a rotation to a solution as close to the target as possible was carried out. As an additional check, we also conducted factor analyses for 4, 5, and 7 factors.

The RMSEAs, measuring goodness of fit, for the factor solutions were as follows: 4 factors = .072, 5 factors = .067, 6 factors = .058, and 7 factors = .060. The RMSEA values for the 4 and 5 factor solutions were unsatisfactory (scores  $\leq .05$ -.06 are judged acceptable). While the RMSEA values for the 6 and 7 factor solutions were both acceptable, the 7 factor solution showed evidence of overfactoring as indicated by the direct quartamin rotation in which there

were two moderate loadings on the seventh factor and the other factor loadings were low, negative values (approximating zero). Therefore, the variance accounted for by the seventh factor was uninterpretable. The 6 factor solution, however, demonstrated high loadings that corresponded to the target and reflected previous findings. Additionally, the confidence intervals corresponding to the target zero loadings generally overlapped with zero and the residuals appeared satisfactory since they did not demonstrate a pattern among the items. These results were not only consistent with previous research but, in fact, indicated no item overlap among the two measures in the present sample.



Table 1

Results of Final HMR Model Examining Correlates of Depressive Symptoms

Step	TR <sup>2</sup>	Beta	t	sr <sup>2</sup>
1. Race	.202	.100	2.06*	.010
Neuroticism		.114	2.06*	.010
2. Debt	.240	.137	2.82**	.018
3. IES-T	.423	.280	4.75***	.052
4. PSS-10	.529	.415	6.78***	.106

Note. N = 209. Abbreviations include: TR<sup>2</sup> = squared multiple correlation for total equation; sr<sup>2</sup> = squared semi-partial correlation; and Debt = major financial difficulty.

\* p < .05.      \*\*p < .01.      \*\*\* p < .0001.

# THE IMPACT OF A PSYCHOLOGICAL/BEHAVIORAL INTERVENTION ON SOCIAL SUPPORT AND ENDOCRINE FUNCTION IN WOMEN WITH BREAST CANCER

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*Background and Methods:* While there is clear evidence that psychological/behavioral interventions with cancer patients provide adjustment and coping benefits (Mark & Meyer, 1995) as well as positive immune and survival benefits (Fawzy et al., 1993; Spiegel et al., 1989), the mechanisms for the benefits of such groups are not clearly understood. We proposed that one of the mechanisms for the success of intervention groups may be through the provision of social support. Thus, by receiving needed support, patients may be "buffered" or protected from the more negative effects of the cancer stressor (e.g., depressive symptoms, Spiker, Trijsburg, & Duivenvoorden, 1997; and immune down-regulation, Andersen et al., 1998). We studied the impact of a psychological/behavioral intervention (26, 1.5 hour long sessions over a year) with stage II or III breast cancer patients, using treatment (intervention) and control (no intervention) arms, on social support and endocrine responses. We were also interested in endocrine functioning as a biological marker of stress severity (Uchino, Cacioppo, & Kiecolt-Glaser, 1996) in breast cancer patients. *Hypotheses:* (1) is an intervention associated with significantly higher levels of social support among the intervention subjects, (2) is an intervention associated with significantly lower endocrine stress responses among intervention subjects, and (3) test the stress buffering hypothesis of social support, that is test for an interaction between study arm (intervention vs. no intervention) and initial level of social support (high vs low) across time (initial vs. post-treatment) on endocrine function (e.g., cortisol). *Results:* Based on results with 100 participants at the 4-month follow-up we find: (1) The intervention participants do not have significantly higher levels of social support than the control subjects. (2) The intervention participants do have significantly fewer depressive symptoms and lower levels of cortisol than the control subjects (Andersen et al., in press). Furthermore, psychological stress (ie., perceived stress and life events), across groups, is associated with depressive symptoms (Golden-Kreutz et al., under review). (3) Participation in the intervention buffers women against the stressful effects (ie., increased cortisol) of multiple group commitments (e.g., social, organizational, etc.). *Conclusions:* These data provide evidence of not only the positive impact of psychological/behavioral interventions on psychological functioning but on endocrine functioning as well in women with breast cancer. The U.S. Army Medical Research and Materiel Command under DAMD17-97-1-7062 supported this work.

# Introduction

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In the context of cancer, social support remains an “important domain of study” (pg. 13, see Helgeson & Cohen, 1996, for a review). Social support is associated with psychological well-being in cancer patients (e.g., Bloom & Spiegel, 1984; Burman & Margolin, 1992). The positive aspects of social support include access to information, understanding, companionship, financial aid, and physical assistance (Cohen & Wills, 1985). Nonetheless, cancer patients may often find social support unavailable, withdrawn, or insufficient (e.g., Bolger et al., 1996; Dakof & Taylor, 1990). Thus, with fewer or a lesser quality of social contacts, they may be left more isolated, more vulnerable to anxiety and depressive symptoms, and may have fewer ways to find resources to facilitate adjustment (Rook & Pietromonaco, 1987). There is clear evidence that psychological/ behavioral interventions with cancer patients provide adjustment and coping benefits (Mark & Meyer, 1995). However, the mechanism for the benefit of such groups is not clearly understood. We proposed that one of the mechanisms for the success of intervention groups may be through the provision of social support. Thus, by receiving needed support, patients may be “buffered” or protected from the more negative effects of the cancer stressor (e.g., depressive symptoms, van’t Spiker et al., 1997).

As cancer diagnosis/treatment is a well-documented stressor (e.g., Andersen, 1992), we were also interested in endocrine functioning as a biological marker of the severity of this stressor (Uchino et al, 1996) in women with breast cancer. An exploration of this relationship is important as acute and chronic stressors are associated with negative changes in the endocrine system (Uchino et al., 1996). Of the small literature (approximately 10 studies) exploring the connections between social support and endocrine function, none have included cancer patients.

## **Hypotheses**

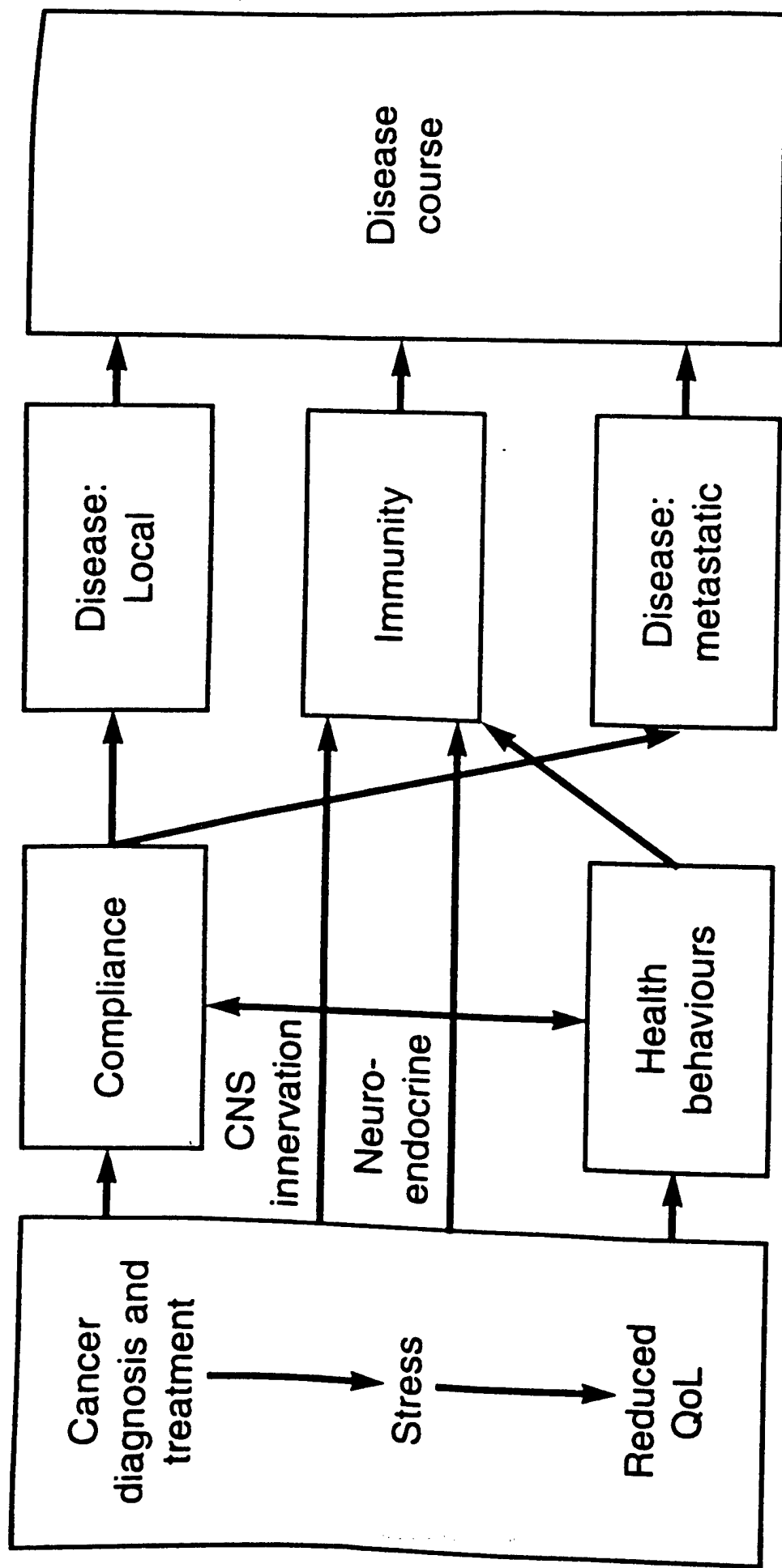
We proposed studying the impact of a psychological/behavioral intervention with breast cancer patients, using treatment (intervention) and control (no intervention) arms, on social support and the endocrine measure, cortisol. We are exploring the following hypotheses:

- 1) Is the intervention associated with significantly higher levels of social support among intervention participants at follow-up.
- 2) Is the intervention associated with a significantly lower cortisol (stress) response among intervention participants at follow-up.
- 3) Is there an interaction between study arm (intervention vs. no intervention) and initial level of social support (high vs. low) across time (initial vs. follow-up) on endocrine function (e.g., cortisol).

**Table 1: Research design. Schematic of the research design for subjects across the 5 years of study participation.**

		YEAR 1				YEARS 2-5		
		Dx./Ca. Trt		Follow up (months)		Continued Follow up (months)		
Grp		0	4	8	12	6	12	
1	x-----	Inten-----x-----Maintenance---x-----Maintenance--x				x		x
2	x-----	None-----x-----None-----x-----None-----x				x		x

Note: Dx. = Cancer diagnosis and Ca.Trt. = Beginning of initial cancer treatment; Inten(sive) = Weekly (x18) intervention sessions with reliability/validity checks on intervention integrity; Maintenance = Monthly (x8) intervention sessions with reliability/validity checks; x = Psychological, health behavior, compliance, and immune, endocrine, and cardiovascular assessments and disease endpoints.



**Figure 1** Theoretical model. A biobehavioral model of the psychological, behavioral, and biologic pathways from cancer stressors to disease course. CNS = central nervous system. From Andersen et al. (1994).

# Method

## Participants and Procedures

Participants ( $N = 116$ ) were accrued from early-1994 to mid-1998 for a larger prospective, longitudinal study (The Stress and Immunity Breast Cancer Project). Sociodemographic characteristics of the sample were as follows: age ( $M = 51$ ;  $SD = 11$ ; range 31-84), race (Caucasian = 88%; African American = 10%; Hispanic 2%), 65% had significant other, years of education ( $M = 15$ ;  $SD = 3$ ; range 10-22), and annual personal income ( $M = \$28,000$ ; range 42,000-110,000). At the time of the initial assessment, all participants had been surgically treated (lumpectomy or mastectomy) within the preceding 3 months for stage II (84%) or stage III (16%) breast cancer but had not yet begun adjuvant treatment (e.g., chemotherapy, radiation). At the four month follow-up, 80% of the sample was actively receiving chemotherapy or radiation. Psychological, behavioral, and medical/ treatment information were conducted at the University's General Clinical Research Center or the breast cancer clinic. All women were paid \$20.00 for each assessment.

## **Measures**

### **Social Support Measures:**

Structural Aspects of Social Support: Presence/Absence of Significant Other; Social Network Index (Berkman, 1979)- Total score and Subscales: Number of Family Members Available for Support, Number of Friends Available for Support, and Number of Groups Belong To (e.g., professional, organizational, social, etc).

Functional Aspects of Social Support: Perceived Support from Family and Friends (Procidano & Heller, 1973).

**Endocrine Measure:** Plasma cortisol. Cortisol was measured using chemiluminescence technology (Nichols Institute San Juan Capistrano, CA). The sensitivity of the assay (0.8 up/dl) was adequate to measure cortisol in each sample. Large cortisol assays (usually 2 cohorts of 20 Ss each with four assessment time points) were run to eliminate interassay variation. The inter and intra assay coefficient variations of the assay were less than 8%.

### **Analytic Approach**

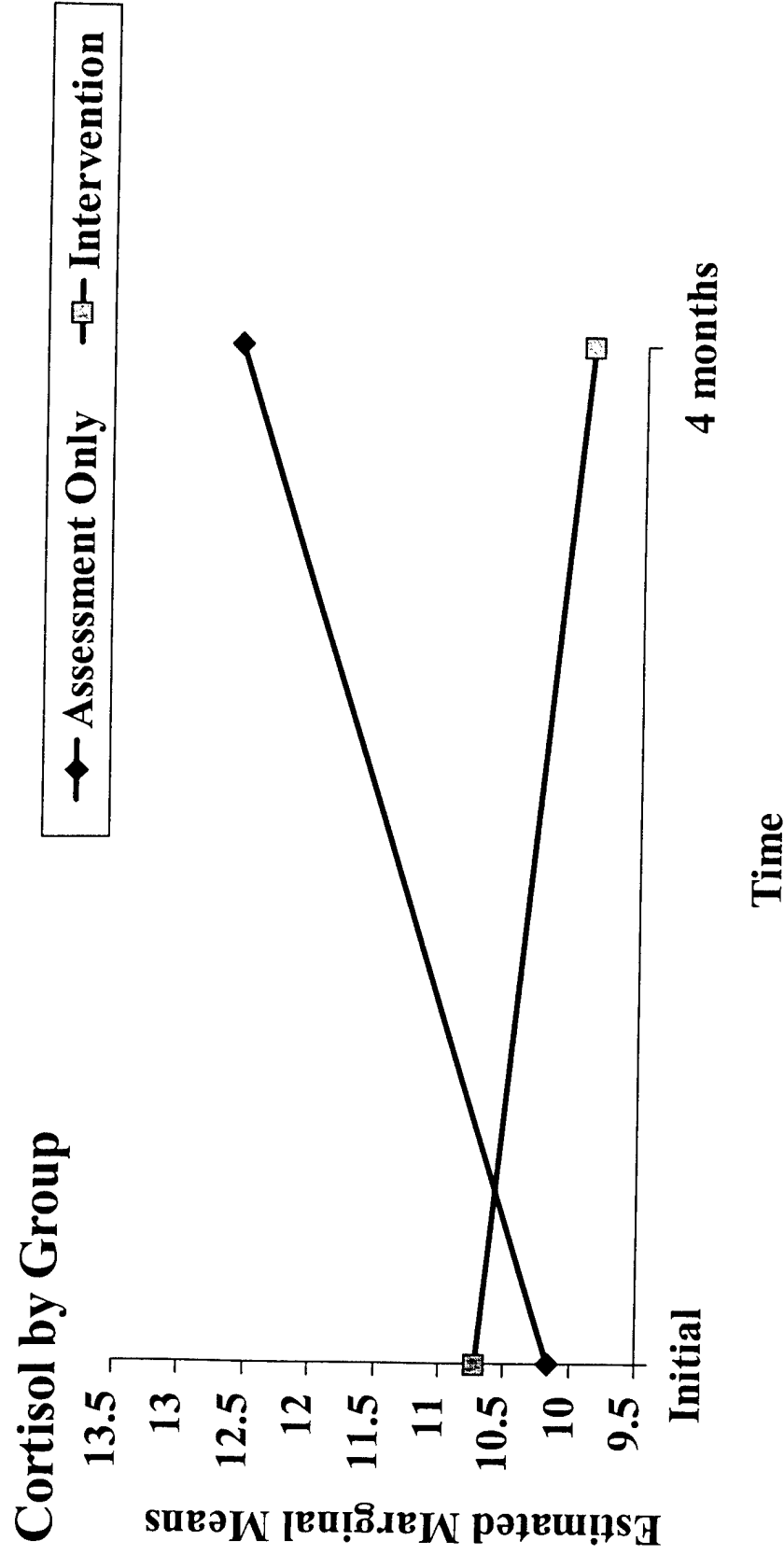
To test for significant group differences over time (initial to 4-nonth assessment), 2X2 repeated measures anovas (group by time) were used with social support and cortisol as the outcomes. For dypothesis 3, we had a 2X2X2 design, group by time by social support esting for changes in cortisol.



### **Intervention**

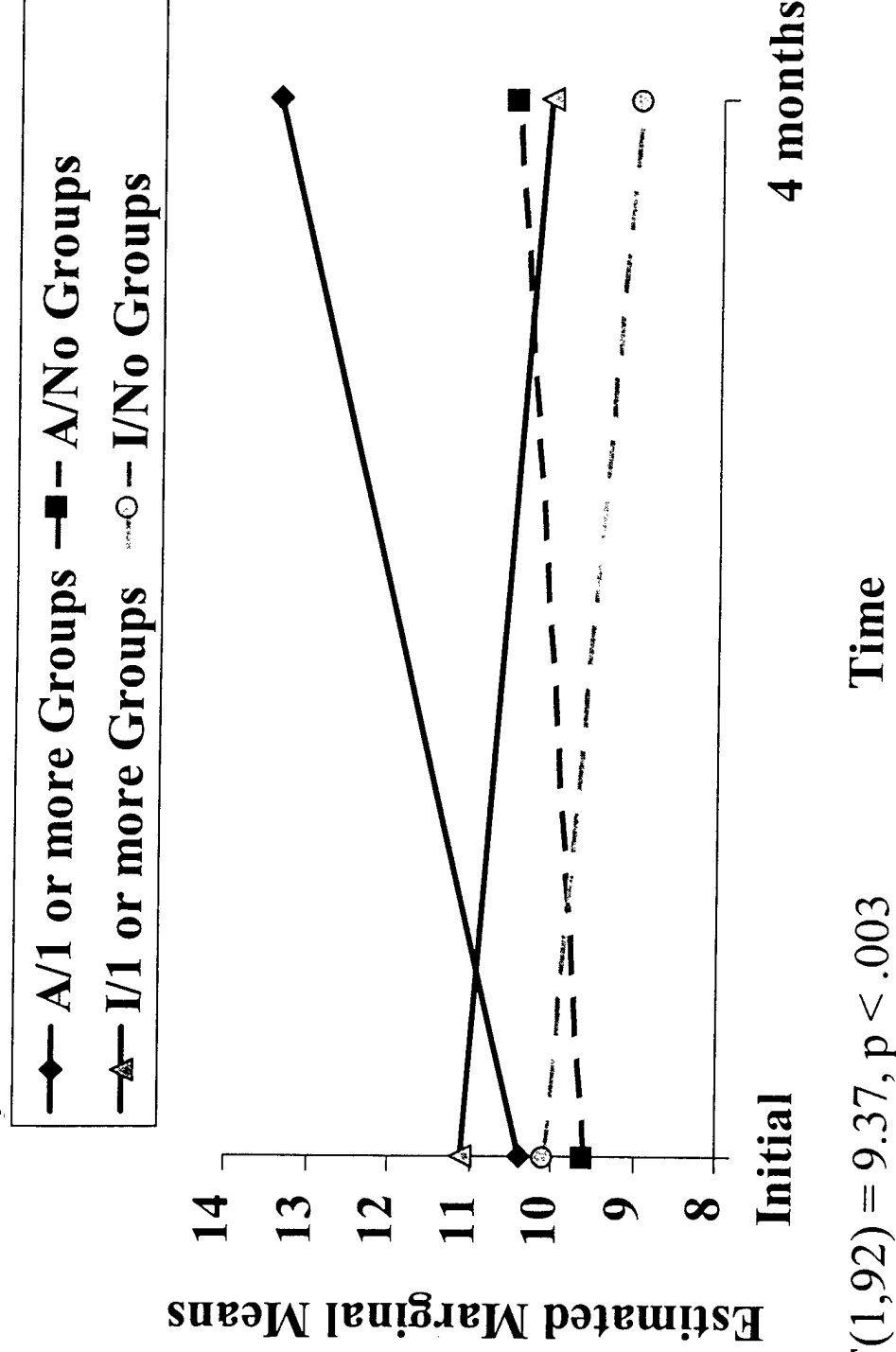
Women were randomized (stratified by tumor size/number of positive lymph nodes, estrogen receptor status, menopausal status, and marital status) between the psychological/behavioral intervention and no intervention (control) arms. The two-phase intervention consists of an intensive phase of weekly meetings for four months and a subsequent maintenance phase of monthly meetings for eight months. Table 1 provides a schematic of the assessment schedule. The intervention components include disease/treatment information, progressive muscle relaxation training, social support identification/usage, assertive communication skills training, body image and sexuality issues, and improving health behaviors (treatment compliance, diet, exercise). The intervention was designed to test a biobehavioral model of cancer stress and disease course (Andersen et al., 1994). This model includes psychological (stress and quality of life), behavioral (health behaviors and compliance), and biologic (endocrine and immune) factors, and specifies the pathways by which health outcomes (e.g., disease endpoints – recurrence, disease free interval) might be affected. See Figure 1 for a diagram of the model.

# Hypothesis 2: Cortisol Differences



$F(1,95) = 8.69, p < .005$

# Hypothesis 3: Interaction Effects



# Results

We have run analyses on all three of our hypotheses proposed for study using the initial and 4-month follow-up data. We will continue to run analyses using the 8 and 12-month follow-up data as our endocrine data becomes available and is added to the data set.

**Hypothesis 1:** Is the intervention associated with significantly higher levels of social support among intervention participants at follow-up? Correlations between the group and social support variables were conducted. Four of the variables, Social Network Index-Total Score, Number of Friends Available for Support, Number of Groups Belong To, and Perceived Support from Friends, were positively correlated with the group variable at  $p < .05$ . These variables were then tested with the repeated measures model. However, none of the analyses were significant at  $p < .05$ , all  $F$ 's  $\leq 3.12$ . Thus, at the 4-month follow-up the intervention group did not report significantly greater perceived social support or greater support availability.

**Hypothesis 2:** Is the intervention associated with significantly lower levels of cortisol among intervention participants at follow-up? The repeated measures anova was significant,  $F(1, 95) = 8.69, p < .005$ . Thus, intervention participants show lowered cortisol over time (means at initial assessment = 10.71; and 4-month follow-up = 9.90) while the assessment only subjects show a significant increase over time (means

at initial assessment = 10.16; and 4-month follow-up = 12.59). This data is shown in the figure Hypothesis 2: Cortisol Differences. (Note: The intervention participants also showed significantly fewer depressive symptoms over time than the assessment only subjects, as measured by the CES-D. Data not shown).

**Hypothesis 3:** Is there an interaction between study arm (intervention vs. no intervention) and initial level of social support (high vs. low) across time (initial vs. follow-up) on endocrine function (e.g., cortisol)? When necessary we converted continuous data into categorical using median splits in order to conduct the anova analyses. While none of the analyses showed a significant three way interaction, one analysis showed two way interaction effects for both the group variable and for the social support variable, Number of Groups Belong To,  $F(1, 92) = 9.37, p < .003$ . These effects are shown in the figure, Hypothesis 3: Interaction Effects. Thus, belonging to more groups was associated with increased cortisol levels at the 4 month follow-up. However, those patients in the intervention showed declines in cortisol whether they belonged to additional groups or not.

# Conclusions

We examined the effects of a psychological/behavioral intervention on social support and endocrine function, namely cortisol, in a sample of 116 women with stage II or III breast cancer. We found at the 4 month follow-up, the time point at which the intensive phase (weekly meetings) of the intervention ended the following results:

- (1) The intervention participants did not have greater availability of support or greater perceptions of support than the control patients.
- (2) However, the intervention participants demonstrated a lowering of their cortisol stress response over the intensive phase of the intervention during which time the control subjects showed a significant increase.
- (3) The more groups women with breast cancer belong to, the more likely they are to demonstrate a cortisol stress response. It may be that the number of commitments during active treatment does not result in the opportunity for the receipt of support from others but rather is an additional burden or stressor. However, participation in an intervention designed to enhance coping and decrease stress appears to lessen stress over time regardless of other group commitments.

These findings verify the benefits of participating in specifically designed interventions structured to meet the needs of women with breast cancer. Further research is being conducted as part of this project to determine if this lowering of cortisol is maintained throughout the entire intervention of one year and what, if any, role such a response plays in disease outcomes (e.g., time to recurrence).

## **Author Note**

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